

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

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## REMARKS/ARGUMENTS

### STATUS OF THE CLAIMS

Claims 1, 3-10, 13-19, 21-56, 59-61, and 201-221 are pending with entry of this amendment, claims 14-17 and 201-221 having been withdrawn and claims 2, 11-12, 20, 57-58, 62-200, and 222-303 having been cancelled. Claims 1, 3-10, 18, 21, 29, 36, 45, 47, 52, 59, and 61 are amended herein. These amendments introduce no new matter and support is replete throughout the specification. These amendments are made without prejudice to renewal of the claims in their original form and are not to be construed as abandonment or dedication of the previously claimed subject matter or agreement with any objection or rejection of record.

As an initial matter, Applicants would like to thank the Examiner and the Supervisory Patent Examiner for the courtesy extended to the undersigned in conducting an interview with the Examiner and the Supervisory Patent Examiner on October 17, 2006, in which the wording of the independent claims and the art by Barrett et al. and Glickman et al. was discussed with the Examiner. The claims have been amended as discussed in the interview.

Claims 1, 21, 29, 36, and 45 have been amended as discussed with the Examiner to recite that the compositions include the enzyme. Support for the amendments can be found throughout the specification, for example, at paragraphs [0009], [0204], and [0294]-[0296], as well as in claim 11 as originally filed.

Applicants also thank the Examiner for the courtesy extended to the undersigned in conducting an interview with the Examiner on December 13, 2006, in which the Examiner indicated that the amendment submitted November 8, 2006, would not be entered. The Examiner indicated that the proposed amendment to claim 1 would overcome the 112 rejection and that the arguments overcame the art rejections, but that the proposed amendment to claim 2 would necessitate further search. The Examiner further indicated that an amendment like that presented but canceling claim 2 would be entered, and that the Examiner would then either allow the case or reopen prosecution.

Accordingly, in the interest of expediting prosecution, Applicants have canceled claim 2, canceled claims that depended only from claim 2, and amended claims that depended from claim 1 or claim 2 to depend only from claim 1. However, Applicants do not

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

concede to the Examiner's rejections and note their intention to file a continuation to pursue the canceled claims. These amendments are therefore made without prejudice to renewal of the claims in their original form and are not to be construed as abandonment or dedication of the previously claimed subject matter or agreement with any objection or rejection of record.

Applicants submit that no new matter has been added to the application by way of the above claim amendments. Accordingly, entry of the Amendment is respectfully requested.

The Examiner requested in a followup discussion to the interview of October 17, 2006 that Applicants point out support in the specification for how the first caging groups are associated with the one or more molecule comprising the substrate. Applicants note that support can be found, for example, at paragraphs [0012], [0150]-[0152], [0209], and [0353]-[0356], which describe, *inter alia*, both covalent and non-covalent association of caging groups. Exemplary embodiments in which caging groups are covalently attached to the substrate are described, for example, in paragraphs [0414]-[0419] and [0427] and schematically illustrated in Figures 6-11 and 17.

Applicants note with appreciation the Examiner's indication of allowable subject matter.

The action of July 12, 2006 included: rejections for alleged indefiniteness (item 2), rejections for alleged anticipation (item 3), rejections for alleged obviousness (items 4-6), response to arguments (items 7-1), and indication of allowable subject matter (item 2). Applicants traverse all rejections and objections, to the extent that they may be applied to the amended claims, for the reasons noted herein.

THE CLAIMS, AS AMENDED, ARE DEFINITE (ACTION ITEM 2)

35 USC §112, Paragraph 2 Rejection of Claims 1-11, 13, and 18-61

Claims 1-11, 13, and 18-61 were rejected for alleged indefiniteness because it was allegedly unclear whether an enzyme is required as part of the composition, and, if not, how the substrate can be converted into a second state from the first state, and whether enzyme activity can be detected without the enzyme. To the extent that the rejections are applied to the amended claims, Applicants traverse.

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

Applicants maintain that, as detailed in the response to the previous Action, a compound known to be a substrate for a particular enzyme is readily recognized as such, regardless of whether the enzyme is present, and thus the composition need not include the enzyme for the meaning of the claims to be clear. However, in the interest of expediting prosecution, Applicants have amended claims 1, 21, 29, 36, and 45 as discussed with the Examiner to specify that the compositions include the enzyme. Claims 2, 11, and 57-58 have been canceled as noted above, rendering the rejection moot with respect to these claims.

Accordingly, Applicants respectfully request that the rejections be withdrawn.

**THE CLAIMS ARE FREE OF BARRETT (ACTION ITEM 3)**

Claims 2 and 57-60 were rejected for alleged anticipation under 35 USC 102(b) by Barrett et al. Applicants respectfully traverse these rejections, to the extent that they may be applied to the amended claims.

As noted above, in the interest of expediting prosecution, Applicants have canceled claim 2 and its dependent claims 57-58, rendering the rejection moot with respect to these claims. Claim 59-60 have been amended to depend only from claim 1. Because independent claim 1 is not anticipated by Barrett et al., it is not necessary to address additional points of distinction between dependent claims 59-60 and Barrett.

Applicants respectfully request that the rejections be withdrawn.

**THE CLAIMS ARE NOT OBVIOUS (ACTION ITEMS 4-6)**

**Item 6**

Claims 1-11 and 18 were rejected for alleged obviousness under 35 USC 103(a) over Glickman et al. in view of Burbaum et al. To the extent that the rejections are applied to the amended claims, Applicants respectfully traverse these rejections.

Three requirements must be met for a *prima facie* case of obviousness. First, the prior art reference(s) must teach all of the limitations of the claims (M.P.E.P. § 2143.03). Second, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention (M.P.E.P. § 2143.01). Third, a reasonable expectation of success is required (M.P.E.P. § 2143.02). The teaching or suggestion to combine and the

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

expectation of success must be both found in the prior art and not based on Applicants' disclosure (M.P.E.P. §2143).

The combination of Glickman et al. and Burbaum et al. does not meet the requirements for a *prima facie* case of obviousness. First, the combination does not teach all the limitations of the claims.

As discussed with the Examiner, Glickman et al. teach a sandwich assay for measuring tyrosine kinase activity in which tyrosine-phosphorylated substrates are captured on a solid support coated with a first anti-phosphotyrosine antibody. A second anti-phosphotyrosine antibody, which is labeled, is then bound to the phosphorylated substrates captured on the support, capturing the second labeled antibody on the support. Unbound second labeled antibody is removed, and the amount of second labeled antibody bound to the solid support is measured. Glickman et al. thus describe an assay that relies on capture on a solid support.

Claim 1 specifies that the composition includes a cell comprising the caged sensor. As discussed with the Examiner, the assay of Glickman et al. is not performed in a cell. Glickman et al. state that the sample to be assayed may be a purified kinase, a cell fraction, a cell or tissue extract, or a bodily fluid (see column 2 lines 56-59). Further, Glickman et al. state that "Where the biological sample is a preparation of whole cells, prior to assay, the cells to be evaluated are lysed..." (column 5 lines 63-65). As discussed with the Examiner, the support-bound compositions formed during the assay of Glickman et al. are clearly not inside a cell, and Glickman et al. fail to teach a cell comprising a sensor.

Furthermore, Applicants maintain that Glickman et al. do not teach a first label that exhibits a first signal when the substrate is in its first state and a second, distinguishable signal when the substrate is in its second state, as is specified in claim 1. The label on the second antibody of Glickman et al. exhibits the same signal regardless of the phosphorylation state of the substrate. The label is merely either bound or not bound to the solid support; it is not responsive to the state of the substrate.

Since Glickman et al. fail to teach at least a cell comprising a sensor, merely adding the caging group from the caged substrate of Burbaum et al. to the substrate and

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

labeled antibody of Glickman does not result in a cell comprising a caged sensor such as that specified in claim 1.

Additional points of distinction are present in the dependent claims, but because independent claim 1 is not anticipated, it is not necessary to address each additional point. Claims 2 and 11-12 have been canceled as noted above, rendering the rejection moot with respect to these claims.

The combination of Glickman et al. and Burbaum et al. does not teach all the limitations of the claims. Specifically, at least the following limitations are simply not taught by the combination: a cell comprising a caged sensor, and a first label whose signal is responsive to the state of the substrate. Furthermore, motivation to combine the teachings of the references is lacking. No suggestion to combine the teachings is found in the references. In addition, there is no reasonable expectation of success, since the suggested combination does not result in the present invention. Applicants respectfully request that the rejections be reconsidered and withdrawn.

Item 7

Claims 13, 19, and 61 were rejected for alleged obviousness under 35 USC 103(a) over Glickman et al. in view of Burbaum et al. further in view of Kris et al. To the extent that the rejections are applied to the amended claims, Applicants respectfully traverse these rejections.

The combination of Glickman et al., Burbaum et al., and Kris et al. does not meet the requirements for a *prima facie* case of obviousness. For example, the combination does not teach all the limitations of the claims.

As described above, the combination of Glickman et al. and Burbaum et al. fails to teach all the limitations of claim 1, from which the claims at issue depend. For example, the combination of Glickman and Burbaum fails to teach at least a cell comprising a caged sensor or a first label whose signal is responsive to the state of the substrate. Merely adding instructions for use in a kit or the identity of the enzyme as a protease from Kris et al. does not result in the claimed invention: the combination still fails to teach at least a first label whose signal is responsive to the state of the substrate or a cell comprising a caged sensor. Moreover, motivation to combine the teachings of the references is lacking. No

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
Reply to Office action of July 12, 2006

suggestion to combine the teachings is found in the references. In addition, there is no reasonable expectation of success, since the suggested combination does not result in the present invention. Accordingly, Applicants respectfully request that the rejections be withdrawn.

Item 8

Claims 47-49 and 52-54 were rejected for alleged obviousness under 35 USC 103(a) over Glickman et al. in view of Burbaum et al. further in view of Fischer et al. To the extent that the rejections are applied to the amended claims, Applicants respectfully traverse these rejections.

The combination of Glickman et al., Burbaum et al., and Fischer et al. does not meet the requirements for a *prima facie* case of obviousness. For example, the combination does not teach all the limitations of the claims.

As described above, the combination of Glickman et al. and Burbaum et al. fails to teach all the limitations of claim 1, from which the claims at issue depend. For example, the combination of Glickman and Burbaum fails to teach at least a cell comprising a caged sensor or a first label whose signal is responsive to the state of the substrate. Merely adding a cellular or subcellular delivery module from Fischer et al. does not result in the claimed invention; the combination still fails to teach at least a first label whose signal is responsive to the state of the substrate or a cell comprising a caged sensor.

In addition, motivation to combine the teachings of the references is lacking. No suggestion to combine the teachings is found in the references. Furthermore, there is no reasonable expectation of success, since the suggested combination does not result in the present invention. Accordingly, Applicants respectfully request that the rejections be withdrawn.

**CONCLUSION**

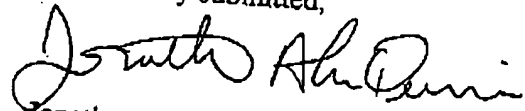
In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Appl. No. 10/716,174  
Amdt. Dated December 13, 2006  
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If the claims are deemed not to be in condition for allowance after consideration of this Response, an interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 337-7871 to schedule an interview.

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Respectfully submitted,



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Attachments:

- 1) A petition to extend the period of response for three months;
- 2) A fax transmittal sheet;

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